



**University of
Zurich**^{UZH}

**Zurich Open Repository and
Archive**

University of Zurich
University Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2019

A protocol for developing, disseminating, and implementing a core outcome set for stress urinary incontinence

Rada, Maria-Patricia ; Pergialiotis, Vasilios ; Betschart, Cornelia ; Falconi, Gabriele ; Haddad, Jorge Milhem ; Doumouchtsis, Stergios K

Abstract: **INTRODUCTION** Randomized trials evaluating interventions for stress urinary incontinence (SUI) have been using variable outcome measures, reporting a variety of outcomes. Alongside this variation across studies, outcome-reporting flaws contribute to a limited use of research to inform clinical practice. The development and use of core outcome sets (COSs) in future trials would ensure that outcomes important to different stakeholders and primarily women with SUI are reported more consistently and comprehensively. **METHODS** An international steering group including healthcare professionals, researchers, and women with urinary incontinence will guide the development of this COS. Potential outcomes will be identified through comprehensive literature reviews. These outcomes will be entered into an international, multiperspective online Delphi survey. All key stakeholders, including healthcare professionals, researchers, and women with urinary incontinence, will be invited to participate. The modified Delphi method encourages stakeholder group convergence toward collective agreement, also referred as consensus, core outcomes. **DISCUSSION** Dissemination and implementation of the resulting COS within an international context will be promoted and reviewed. Embedding the COS for SUI within future clinical trials, systematic reviews and clinical practice guidelines could make a significant contribution to advancing the value of research in informing clinical practice, enhancing patient care and improving outcomes. The infrastructure created by developing a COS for SUI could be leveraged in other settings, for example, selecting research priorities and clinical practice guideline development.

DOI: <https://doi.org/10.1097/MD.00000000000016876>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-180747>

Journal Article

Published Version



The following work is licensed under a Creative Commons: Attribution 4.0 International (CC BY 4.0) License.

Originally published at:

Rada, Maria-Patricia; Pergialiotis, Vasilios; Betschart, Cornelia; Falconi, Gabriele; Haddad, Jorge Milhem; Doumouchtsis, Stergios K (2019). A protocol for developing, disseminating, and implementing a core outcome set for stress urinary incontinence. *Medicine*, 98(37):e16876.

DOI: <https://doi.org/10.1097/MD.00000000000016876>

A protocol for developing, disseminating, and implementing a core outcome set for stress urinary incontinence

Maria-Patricia Rada, MD^{a,b,*}, Vasilios Pergialiotis, MD, PhD^c, Cornelia Betschart, MD^d, Gabriele Falconi, MD^e, Jorge Milhem Haddad, MD^f, Stergios K. Doumouchtsis, MSc, MPH, PhD, FRCOG^{a,c,g}

Abstract

Introduction: Randomized trials evaluating interventions for stress urinary incontinence (SUI) have been using variable outcome measures, reporting a variety of outcomes. Alongside this variation across studies, outcome-reporting flaws contribute to a limited use of research to inform clinical practice. The development and use of core outcome sets (COSs) in future trials would ensure that outcomes important to different stakeholders and primarily women with SUI are reported more consistently and comprehensively.

Methods: An international steering group including healthcare professionals, researchers, and women with urinary incontinence will guide the development of this COS. Potential outcomes will be identified through comprehensive literature reviews. These outcomes will be entered into an international, multiperspective online Delphi survey. All key stakeholders, including healthcare professionals, researchers, and women with urinary incontinence, will be invited to participate. The modified Delphi method encourages stakeholder group convergence toward collective agreement, also referred as consensus, core outcomes.

Discussion: Dissemination and implementation of the resulting COS within an international context will be promoted and reviewed. Embedding the COS for SUI within future clinical trials, systematic reviews and clinical practice guidelines could make a significant contribution to advancing the value of research in informing clinical practice, enhancing patient care and improving outcomes. The infrastructure created by developing a COS for SUI could be leveraged in other settings, for example, selecting research priorities and clinical practice guideline development.

Abbreviations: COMET = Core Outcome Measures in Effectiveness Trials, COS = core outcome set, COS-STAR = COS-Standards for Reporting, CROWN = The Core Outcomes in Women's Health, ICHORSUWH = International Collaboration for Harmonising Outcomes, Research, and Standards in Urogynaecology and Women's Health, SUI = stress urinary incontinence.

Keywords: core outcome set, delphi survey, randomised controlled trials, stress urinary incontinence

Funding: This research was funded by a United Kingdom Continence Society grant (12.04.2018). The grant aims to cover the following expenses: patient and public participation, teleconference, web-based Delphi survey.

The authors report no conflicts of interest.

Supplemental Digital Content is available for this article.

^a Department of Obstetrics and Gynaecology, Epsom & St Helier University Hospitals NHS Trust, London, United Kingdom, ^b "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, 2nd Department of Obstetrics and Gynaecology, "Dominic Stanca" Clinic, Romania, ^c Laboratory of Experimental Surgery and Surgical Research N S Christeas, Athens University Medical School, Athens, Greece, ^d Department of Gynecology, University Hospital of Zurich, Zurich, Switzerland, ^e Department of Obstetrics and Gynaecology, San Bortolo Hospital, Vicenza, Italy, ^f Department Obstetrics and Gynaecology, Urogynaecology Division, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, ^g St George's University of London, London, UK.

* Correspondence: Maria-Patricia Rada, Epsom General Hospital, Epsom, United Kingdom (e-mail: mpr1388@gmail.com).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Rada MP, Pergialiotis V, Betschart C, Falconi G, Haddad JM, Doumouchtsis SK, CHORUS, an International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's Health (i-chorus.org). A protocol for developing, disseminating, and implementing a core outcome set for stress urinary incontinence. *Medicine* 2019;98:37(e16876).

Received: 22 July 2019 / Accepted: 25 July 2019

<http://dx.doi.org/10.1097/MD.00000000000016876>

1. Introduction

Stress urinary incontinence (SUI) affects millions of women worldwide.^[1] Short- and long-term associated morbidity may have an effect on quality of life including daily activities, psychological wellbeing, and sexual function. The efficacy of the surgical and nonsurgical options to treat SUI has been studied in various clinical trials^[2–5]; however, commonly and highly effective surgical treatments, such as the mid-urethral slings, are under scrutiny in the UK, Republic of Ireland, and elsewhere.

Current evidence has major flaws. In the absence of a standardized approach in research methodology, most SUI trials have reported information on various outcomes. For example, safety aspects of potential treatments for SUI, particularly over the longer term, were inconsistently evaluated across clinical trials. Even in the unlikely situation where outcomes have been consistently collected, evidence synthesis can be limited by the use of different outcome measures, including definitions and measurement instruments.

Potential new treatments for SUI require an effective evaluation. The reporting of appropriate outcomes to reflect efficacy and safety of a treatment is a critical step in designing future randomized trials.^[6] To ensure relevance to policy and practice, the chosen outcomes need to be relevant to key stakeholders (Fig. 1).

The development and use of a collection of well-defined, discriminatory and feasible outcomes, termed a COS, would help to address these issues.^[7] COS are minimum datasets that can be

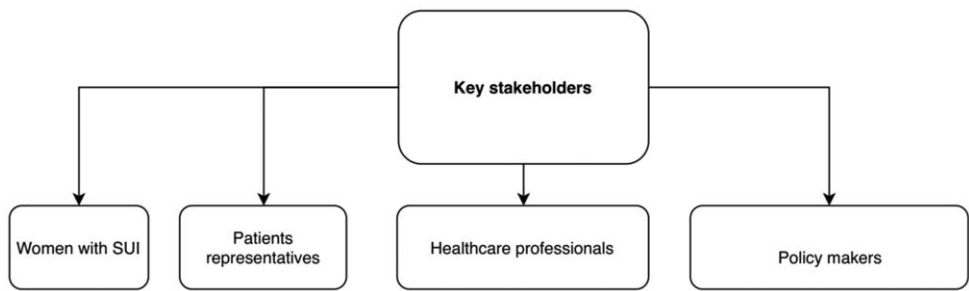


Figure 1. Key stakeholders involved in SUI. SUI=stress urinary incontinence.

measured in a standardized manner and reported consistently in the final publication.

Our aim is to produce, disseminate, and implement a COS for SUI according to the Core Outcome Measures in Effectiveness Trials (COMET) guidelines,^[8] following the pathway illustrated by Figure 2.

2. Methods

2.1. Prospective registration

This study has been prospectively registered with the COMET initiative (registration number: 981) and is available online (www.comet-initiative.org/studies/details/981). This project is led and conducted by CHORUS, An International Collaboration

for Harmonising Outcomes, Research, and Standards in Urogynaecology and Women’s Health (<https://i-chorus.org/>).

2.2. Creating an international group for the development of a COS for SUI

An international steering group including healthcare professionals, researchers and women with SUI will guide the development of a COS that will be applicable to clinical studies evaluating therapeutic interventions for women with SUI. The development of effective interventions to reduce the effect of SUI on women’s quality of life is urgently required, given the flaws and weaknesses documented in Cochrane reviews.^[6–7,9] Also, the scrutiny that previously considered “criterion standard” procedures such as the mid-urethral slings are currently undergoing by government

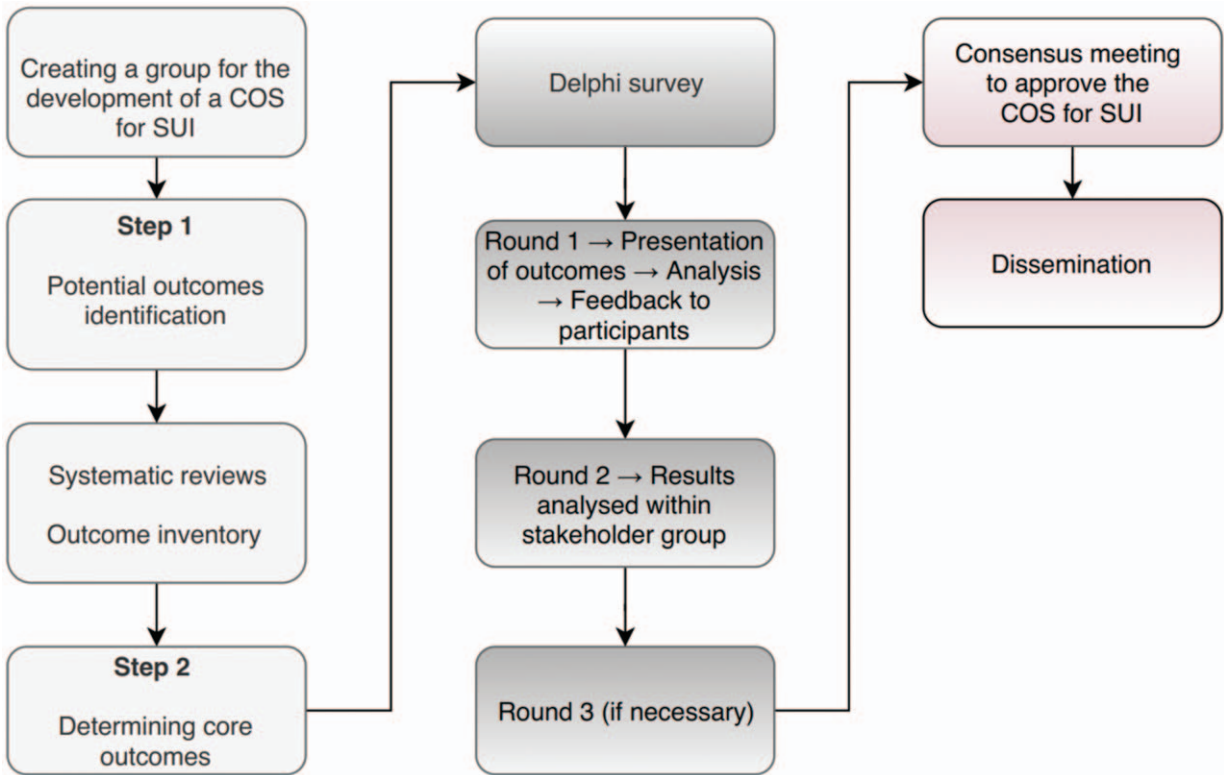


Figure 2. The steps of developing a COS for SUI. COS=core outcome set; SUI=stress urinary incontinence.

bodies in the UK and Republic of Ireland resulted in a current high vigilance regime of restricted practice.^[10–11]

2.3. Step 1: identifying potential outcomes

Selection of appropriate outcomes is an essential step for study design, as ultimately any study is only as valuable as its endpoints.^[8] Clinical trials that evaluate benefits and harms of interventions for SUI must select outcomes of relevance to key stakeholders and measure them using adequate tools. The main issues that arise throughout this process are inconsistent selection, measurement, and reporting of outcomes. A significant challenge is represented by the measurement of outcomes of interventions for SUI in a variety of ways that finally leads to outcome reporting bias. Therefore, the barrier to compare and highlight differences in clinical trials' findings has an inevitable negative effect on their interpretation and embedding in clinical practice.

One way to address these issues is by going through a multi-step pathway (Fig. 2) that has been successfully applied in several disciplines, to develop, disseminate, and implement COS for various conditions. This protocol is in line with the COMET Initiative guidelines and other COS development research relevant to women's health including preeclampsia, endometriosis, pelvic organ prolapse, among others.^[7,12–14]

For the development of this protocol and to evaluate the extent of existing variations we are currently completing a systematic review on the variation of outcomes and outcome measures in SUI randomised trials and we will generate an inventory of outcomes, outcome measures and definitions of both to inform the consensus process. The results will be entered into a modified Delphi method. Through the review we also aim to increase the range of evidence synthesis in SUI interventions field and to guide further research conduct towards the development of a COS.

2.3.1. Systematic review (previously reported outcomes).

We identified trials evaluating therapeutic interventions for SUI following a standardized methodology and searches of databases including PubMed/ Medline, EMBASE, and Cochrane Central Register of Controlled Trials. We will evaluate publications that aim to improve the health of women with SUI, including trials and guidelines on various treatments including surgical interventions, physical therapies, and behavioral approaches.

2.3.2. Outcome inventory. A comprehensive inventory of outcomes identified by systematic reviews will be developed. Outcome domains will be listed in a database and coded according to the taxonomy proposed by the COMET Initiative.

If there is uncertainty as to how to classify or present an outcome, consensus of the steering group will be sought. Following the steering group's agreement, the outcome inventory will be entered into the modified Delphi method.

2.4. Step 2: determining core outcomes

Delphi method involves a series of supervised rounds of surveys. The modified Delphi method encourages repeated reflection and rescoring of outcomes.^[15] These actions promote whole and individual stakeholder group convergence upon a consensus of core outcomes and has advantages over other agreement methods less standardized. Web-based Delphi surveys facilitate international participation and are considered feasible and efficient.^[16]

Key stakeholders will be invited to participate in the Delphi survey. Stakeholders' selection is meant to ensure inclusion of all relevant parties with an interest in SUI interventions. As there are no clear recommendations that we are aware of for the optimum sample size^[16] for a Delphi survey, based upon previous studies, we will aim to include 20 participants from each stakeholder group to ensure adequate representation.

The results of round 1 responder participants in each stakeholder group will be assessed at the end of this round. They will be presented as total number and/or percentage of:

- registrations
- respondents who have completed the survey
- respondents who completed the round
- respondents in each stakeholder group
- respondents compared to potential respondents as identified from the information provided by clinical leads
- new respondents who were not included in original invitation to complete the survey.

2.4.1. Round 1. Participants will be invited to register online, provide demographic details, and commit to all rounds.^[17] They will be allocated a unique identifier which will make their responses anonymous. Individual outcomes will be scored by participants using a 7-point Likert Scale anchored between 1 (not important) and 7 (critical). This scale has been widely adopted by COS developers.^[18] During the first round, participants will be invited to suggest additional outcomes. Instead of limiting the variety of outcomes measured and reported across studies, a core outcome set would establish minimal reporting requirements while considering individual aspects. Additional outcomes noted by participants will be reviewed by the outcome committee and, if novel, listed in round 2. The round will close following a 4-week window.

2.4.2. Round 2. Participants will present their individual and stakeholder group responses and they will be invited to reflect on the observed similarities and differences before proceeding to the next step and scoring individual outcomes again. The round will close following a 4-week window.

For each outcome, the median and H-spread of scores will be summarized graphically by stakeholder group and individual responses. Rescoring outcomes as part of the modified Delphi method facilitates agreement upon core outcomes.^[19] The round's 2 results will be reviewed and analyzed by the steering group to consider the need for a further Delphi survey round.

This round's results, as well as the results of any potential further round, will enable individual outcomes to be classified as shown in Table 1.^[16] Although subjective, these definitions and criteria have been proposed by previous COS developers,^[16,20–21] and help collecting and reporting uniform results.

2.5. Stakeholder consultation

This final phase will involve a face-to-face meeting with key stakeholders and viewpoints from participants who have completed all steps of the survey. The objective of the consensus meeting will be to discuss consensus outcomes and approve a final COS for SUI interventions. During this meeting, the results from each round of the Delphi survey will be presented. To avoid biased consensus formation among group participants, the steering committee will ensure that the meeting is interactive

Table 1**Consensus status based on core outcome criteria.**

Consensus status	Description	Criteria
Consensus in	Classify as a core outcome	Over 70% of participants in each stakeholder group score this outcome domain "critical" AND Less than 15% of participants in each stakeholder group score outcome domain "not important."
Consensus out	Do not classify as a core outcome	Over 70% of participants in each stakeholder group score outcome domain "not important" AND Less than 15% of participants in each stakeholder group score outcome domain "critical."
Lack of consensus	Do not classify as a core outcome	Anything else

and considers all opinions. To facilitate dissemination and implementation, professional society representatives, editors from key journals, and funders of SUI research^[22–23] will be invited to take part in this meeting.

3. Discussion

As with previous COS development projects, this project is not directly influencing patient safety,^[12,24–25] and therefore, ethics approval was not required. Also, The Medical Research Council decision tool that helps to determine whether a research project conducted within the UK requires approval from an NHS Research Ethics Committee (REC) indicated that this research does not require REC approval.

All involved participants will be asked for their consent (Supplemental Digital Content (Appendix 1, <http://links.lww.com/MD/D220>)) before participating in either stakeholder meetings or the Delphi survey and all procedures will be conducted according to the Declaration of Helsinki.^[25] A "no-response" option will be allowed both for the survey and interactive parts of the research to ensure responder's right to withhold information. A specific timeframe of the Delphi process will be provided and information concerning the interval of data storage and handling will be made available to participants.

This COS development protocol will follow COS-Standards for Reporting (COS-STAR) statement and checklist.^[26] As dissemination is the crucial step in the effective application of trial outcomes, awareness must be increased among all involved parties to ensure widespread use of this COS in SUI interventions research and proper reporting.

Implementing COS in future clinical studies, systematic reviews and clinical guidelines could make a profound contribution to advancing the reach and relevance of research in informing clinical practice, enhancing patient care and improving intervention outcomes for women suffering from SUI. Mapping all outcomes reported in clinical trials assessing interventions for SUI in women will provide basis for offering best patient care for these patients.

3.1. Improving clinical trial outcome selection

Standard Protocol Items-Recommendations for Interventional Trials (SPIRIT) supported by funders of health research, recommend the use of COS where they exist.^[27] This study protocol was designed to the SPIRIT checklist.^[27] A COS that would hopefully ensure that consensus outcomes important to all stakeholders, including women with SUI are properly collected and reported. When clinical studies use consensus outcomes and outcome measures, meta-analyses, using individual patient data are feasible.

3.2. Improving clinical trial reporting and evidence synthesis

The Core Outcomes in Women's Health (CROWN) initiative, supported by several journals, have already implemented COS.^[23] Participating journals will require authors to report the results for core outcomes within trial reports and systematic reviews and offer conclusions based on these outcomes rather than non-core or surrogate outcomes. Where COSs have not been collected, the authors will be asked to report this limitation and its effect for their findings.^[22]

3.3. Improving clinical practice guidelines

The National Institute for Health and Care Excellence (NICE) supports the use of COS when selecting outcomes during evidence scoping and synthesis.^[8] As this activity forms the basis of updating guideline recommendations, the COS could have a direct effect in improving clinical practice.

Acknowledgments

CHORUS, an International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's Health (i-chorus.org).

Author contributions

Conceptualization: Maria Rada, Vasilios Pergialiotis, Cornelia Betschart, Gabriele Falconi, Jorge Milhem Haddad, Stergios Doumouchtsis.

Funding acquisition: Stergios Doumouchtsis.

Methodology: Maria Rada.

Project administration: Stergios Doumouchtsis.

Resources: Maria Rada, Vasilios Pergialiotis, Cornelia Betschart, Jorge Milhem Haddad, Stergios Doumouchtsis.

Supervision: Stergios Doumouchtsis.

Writing – original draft: Maria Rada, Stergios Doumouchtsis.

Writing – review & editing: Maria Rada, Vasilios Pergialiotis, Cornelia Betschart, Gabriele Falconi, Jorge Milhem Haddad, Stergios Doumouchtsis.

References

- [1] Keltie K, Elneil S, Monga A, et al. Complications following vaginal mesh procedures for stress urinary incontinence: an 8 year study of 92,246 women. *Sci Rep* 2017;7:12015.
- [2] Kirchin V, Page T, Keegan PE, et al. Urethral injection therapy for urinary incontinence in women. *Cochrane Database of Systematic Reviews*. *Cochrane Database Syst Rev* 2017;7:CD003881.
- [3] Ford AA, Rogerson L, Cody JD, et al. Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev* 2017;7:CD006375.

- [4] Dumoulin C, Hay-Smith EJC, MacHabee-Séguin G. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst Rev* 2018;10: CD005654.
- [5] Dumoulin C, Cacciari LP, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst Rev* 2014; CD005654.
- [6] Pergialiotis V, Durnea C, Elfituri A, et al. Do we need a core outcome set for childbirth perineal trauma research? A systematic review of outcome reporting in randomised trials evaluating the management of childbirth trauma. *BJOG* 2018;125:1522–31.
- [7] Duffy JMN, van't Hooft J, Gale C, et al. A protocol for developing, disseminating, and implementing a core outcome set for pre-eclampsia. *Pregnancy Hypertension* 2016;6:274–8. doi: 10.1016/j.preghy.2016.04.008.
- [8] Williamson PR, Altman DG, Bagley H, et al. The COMET Handbook: Version 1.0. *Trials* 2017;18(suppl 3):280.
- [9] Ayeleke RO, Hay-Smith EJC, Omar MI. Pelvic floor muscle training added to another active treatment versus the same active treatment alone for urinary incontinence in women. *Cochrane Database Syst Rev* 2015; CD010551.
- [10] Medicines and Healthcare products Regulatory Agency. Pause on the use of vaginally inserted surgical mesh for stress urinary incontinence. www.gov.uk. Available at: <https://www.gov.uk/government/news/pause-on-the-use-of-vaginally-inserted-surgical-mesh-for-stress-urinary-incontinence>. Accessed: June 16, 2019.
- [11] Royal College of Obstetricians & Gynaecologists. Mesh safety alert. www.rcog.org.uk. Available at: <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/mesh-safety-alert/>. Accessed: June 16, 2019.
- [12] Hirsch M, Duffy JMN, Barker C, et al. Protocol for developing, disseminating and implementing a core outcome set for endometriosis. *BMJ Open* 2016;6:e013998.
- [13] Durnea CM, Pergialiotis V, Duffy JMN, et al. A systematic review of outcome and outcome-measure reporting in randomised trials evaluating surgical interventions for anterior-compartment vaginal prolapse: a call to action to develop a core outcome set. *Int Urogynecol J* 2018;29:1727–45.
- [14] de Mattos Lourenco TR, Pergialiotis V, Duffy JMN, et al. A systematic review on reporting outcomes and outcome measures in trials on synthetic mesh procedures for pelvic organ prolapse: Urgent action is needed to improve quality of research. *Neurourol Urodyn* 2019;38: 509–24.
- [15] Freitas Â, Santana P, Oliveira MD, et al. Indicators for evaluating European population health: A Delphi selection process. *BMC Public Health* 2018;18:557.
- [16] Sinha IP, Smyth RL, Williamson PR. Using the Delphi Technique to Determine Which Outcomes to Measure in Clinical Trials: Recommendations for the Future Based on a Systematic Review of Existing Studies. *PLoS Med* 2011;8:e1000393.
- [17] Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 2011;64:395–400. doi: 10.1016/j.jclinepi.2010.09.012.
- [18] Gopalakrishna G, Mustafa RA, Davenport C, et al. Applying Grading of Recommendations Assessment, Development and Evaluation (GRADE) to diagnostic tests was challenging but doable. *J Clin Epidemiol* 2014;67:760–8.
- [19] Boog B. Qualitative research practice. *Journal of Social Intervention: Theory and Practice* 2005;14:47–9.
- [20] Harman NL, Wilding J, Curry D, et al. Selecting Core Outcomes for Randomised Effectiveness trials In Type 2 Diabetes (SCORE-IT): study protocol for the development of a core outcome set. *Trials* 2018;19:427.
- [21] Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012;13:132.
- [22] Khan K. The CROWN Initiative: journal editors invite researchers to develop core outcomes in women's health. *BJOG* 2014;121:1181–2.
- [23] Khan K, Bent A. The CROWN initiative: Journal editors invite researchers to develop core outcomes in Women's Health: The Core Outcomes in Women's Health Initiative. *Female Pelvic Med Reconstr Surg* 2015;21:1–2.
- [24] Chiarotto A, Deyo RA, Terwee CB, et al. Core outcome domains for clinical trials in non-specific low back pain. *Eur Spine J* 2015;24: 1127–42.
- [25] Ma C, Panaccione R, Fedorak RN, et al. Development of a core outcome set for clinical trials in inflammatory bowel disease: study protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey. *BMJ Open* 2017;7:e016146.
- [26] Kirkham JJ, Gorst S, Altman DG, et al. Core Outcome Set-STAndards for Reporting: The COS-STAR Statement. *PLoS Med* 2016;13:e1002148.
- [27] Chan AW, Tetzlaff JM, Gøtzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346: e7586.